Published in final edited form as:

Obstet Gynecol. 2018 October ; 132(4): 948–955. doi:10.1097/AOG.0000000000002863.

Choice of Prophylactic Antibiotics and Surgical Site Infections After Cesarean Delivery

Tetsuya Kawakita, MD¹, Chun-Chih Huang, PhD^{2,3}, and Helain J. Landy, MD⁴

¹Obstetrics and Gynecology, MedStar Washington Hospital Center, Washington, DC, United States

²Department of Biostatistics and Epidemiology, MedStar Health Research Institute, Hyattsville, MD, United States

³Georgetown-Howard Universities Center for Clinical and Translational Science, Washington, DC, United States

⁴Obstetrics and Gynecology, MedStar Georgetown University Hospital, Washington, DC, United States

Abstract

Objective: To examine the rate of surgical site infection according to the choice of antibiotics in women undergoing cesarean delivery.

Methods: We conducted a retrospective cohort study of women undergoing cesarean delivery (labored, unlabored, and scheduled) from 2012 to 2017. Women with chorioamnionitis and those who did not receive any antibiotics were excluded. Our primary outcome was defined a priori as a composite of cellulitis, endometritis, deep wound infection, abdominopelvic abscess and sepsis. Outcomes were examined according to the choice of antibiotics: cefazolin, standard alternative (both clindamycin and gentamicin), and inappropriate alternatives (such as clindamycin only). Multivariable logistic regression model was used to calculate the propensity score for each observation, which was the probability of receiving a particular antibiotics regimen. The propensity score-adjusted logistic regression models were conducted to calculate adjusted odds ratios (OR) and the 95% confidence intervals (CI). Firth's penalized likelihood approach was applied to address issues of rare events.

Results: Among 6,584 selected women, 6,163 (93.6%), 274 (4.2%), and 147 (2.2%) received cefazolin, standard alternative, and inappropriate alternatives, respectively. Use of standard alternative antibiotics compared to cefazolin was not associated with increased odds of the primary outcome (crude OR 1.50 [0.92–2.46]; adjusted OR 1.63 [0.97–2.60]) but was associated with increased odds of cellulitis (crude OR 2.07 [1.16–3.70]; adjusted OR 1.93 [1.03–3.31]). Use of inappropriate alternative antibiotics compared with cefazolin was associated with increased odds

Corresponding author: Tetsuya Kawakita, MD, 110 Irving Street, NW, 5B45, Washington, DC 20010; tetsuya.x.kawakita@gmail.com.

Financial Disclosure

The authors did not report any potential conflicts of interest.

Each author has indicated that he or she has met the journal's requirements for authorship.

of the primary outcome (crude OR 4.37 [2.80–6.83]; adjusted OR 4.13 [2.59–6.36]) as well as some components of the composite outcome such as endometritis before discharge (crude OR 6.85 [3.94–11.90]; adjusted OR 6.68 [3.69–11.44]) and cellulitis (crude OR 3.36 [1.78–6.34]; aOR 3.23 [1.63–5.81]).

Conclusion: Both standard alternative and inappropriate alternatives were associated with increased odds of surgical site infections compared with cefazolin.

Précis:

Prophylactic use of clindamycin and gentamicin, compared to cefazolin, was associated with increased odds of surgical site infections in women undergoing cesarean delivery.

Introduction

Cesarean delivery is one of the most common procedures performed in the United States, accounting for 32% of all deliveries.¹ Cesarean delivery is associated with wound complications such as wound infection, hematoma/seroma, wound dehiscence, and endometritis.^{2–4} Wound complication, described in 2–16% of women after cesarean delivery, is a significant cause of maternal morbidity and mortality^{3–9} and the major cause of prolonged hospital stay and burden to health care system.^{5, 10} Though the rate of wound complications has declined with routine use of preoperative antibiotics, it still remains a significant clinical concern.⁹

Prophylactic antibiotics are recommended in women undergoing cesarean delivery to decrease the risk of wound infection.¹¹ First line treatment has been first-generation cephalosporins such as cefazolin. For women with significant beta-lactam allergy such as anaphylaxis, angioedema, respiratory distress, or urticaria, the alternative to the first-generation cephalosporin recommended by the American College of Obstetricians and Gynecologists (ACOG) is clindamycin combined with an aminoglycoside.¹¹ However, the efficacy of this alternative antibiotic regimen is not well studied. We hypothesized that prophylactic use of non-cephalosporin antibiotics was associated with increased odds of surgical site infections compared to that of cefazolin. The aim of our study was to examine the rate of surgical site infection in women who received non-cephalosporin antibiotics compared to those with the first generation cephalosporin prophylaxis.

Materials and Methods

This was a retrospective cohort study of all women at 23 weeks of gestation or greater who underwent cesarean delivery (labored, unlabored, and scheduled) at MedStar Washington Hospital Center from January 2012 to December 2017. Women with chorioamnionitis (defined as fever at least 38.0°C plus fetal tachycardia [>160 beats per min] or purulent fluid from cervical os)¹² were excluded since gentamicin and clindamycin were often used therapeutically. Women who did not receive prophylactic antibiotics also were excluded. The electronic medical record was used to identify women who underwent cesarean delivery. The first author (TK) conducted the chart review to obtain data from outpatient, inpatient, and anesthesia records. The MedStar Institutional Review Board approved this study.

At MedStar Washington Hospital Center, antibiotics are given intravenously within 1 hour of skin incision. A 2 gram dose of cefazolin is usually given, but a 3 gram dose is considered for women with body mass index (BMI) 40 kg/m² or greater. The standard intravenous doses of clindamycin and gentamicin are 900 mg and 5 mg/kg, respectively. Since December 2016, intravenous administration of azithromycin 500 mg in addition to cefazolin or clindamycin and gentamicin was implemented for all cesarean deliveries.

Women were first categorized into two groups: women who received prophylactic cefazolin and women who received non-cephalosporin prophylactic antibiotics. The group of women who received non-cephalosporin antibiotics was further stratified into those who received standard alternative antibiotics (both clindamycin and gentamicin), and those who received inappropriate alternative antibiotics (such as clindamycin only, gentamicin only, vancomycin, or ampicillin). For women who received non-cephalosporin antibiotics, we reviewed the status of beta-lactam antibiotics (no allergy; significant beta-lactam allergy such as anaphylaxis, angioedema, respiratory distress, or urticaria; beta-lactam allergy without significant reaction; or beta-lactam allergy with unknown severity).

Maternal demographics (maternal age, parity, multiple gestation, number of prior cesarean deliveries, race/ethnicity, body mass index [BMI] on admission, gestational age, smoking, alcohol use, and illicit drug use), maternal comorbidities including pregestational diabetes, gestational diabetes, chronic hypertension, pregnancy-associated hypertensive disease (gestational hypertension, preeclampsia, hemolysis, elevated liver enzyme, low platelet [HELLP] syndrome, and eclampsia), human immunodeficiency virus (HIV), detailed information about the cesarean delivery (emergency cesarean delivery, administration of azithromycin, skin preparation type, vaginal preparation, skin incision type, skin closure type, and total operative time), and labor information (labor [cervical dilation 4 cm in the setting of contractions], second stage of labor, rupture of membranes, and duration of rupture of membranes) were evaluated. Emergency cesarean delivery was defined as emergent cesarean delivery where skin preparation was not completed due to time constraints reflecting the emergency.

Our primary outcome was defined as a composite of surgical site infections including cellulitis, endometritis, deep wound infection, abdominopelvic abscess and sepsis (blood culture confirmed) within 6 weeks after cesarean delivery. This a priori composite outcome was intended to examine overall infectious morbidities according to the choice of prophylactic antibiotics. Secondary outcomes included hematoma/seroma, wound dehiscence (>1 cm), any main Emergency Department visit during postpartum period, main Emergency Department visit due to wound complication (infection, hematoma/seroma, or dehiscence), and any hospital readmission occurring up to 6 weeks after cesarean delivery. Objective definitions of wound complications were obtained from chart review. Cellulitis was defined as an infection of the skin or subcutaneous tissue with at least one of the following: purulent discharge, organisms isolated from the incision, or erythema/induration/tenderness. Deep wound infection was defined as an infection of deep soft tissues with at least one of the following: purulent discharge, spontaneous dehiscence, or evidence of abscesses. Endometritis was defined as the presence of at least two of the following: fever (>38.0°C), abdominal pain, uterine tenderness, or purulent drainage from the uterus.

Abdominopelvic abscess was confirmed by radiologic findings. Hematoma/seroma was defined as a collection of blood or serum.

Outcomes were compared between women who received cefazolin and those who received non-cephalosporin antibiotics. We used the chi-square test or Fisher's exact test to analyze the categorical variables and Student's t-test for continuous variables. Given potential differences in characteristics between women who received cefazolin and those who received non-cephalosporin antibiotics, we performed a propensity score-adjusted logistic regression. For example, women with beta-lactam allergy have a history of exposure to beta-lactam antibiotics, which could be a marker for unmeasured characteristics that makes women more likely to have surgical site infections. Since the assignment of different use of antibiotics is not by random in clinical practice and it may include unobserved reasons, it is appropriate to compute the propensity score of the treatment option and adjust them in the logistic regression models for analyzing our research question.¹³ Multivariable logistic regression model was used by considering maternal age, race, gestational age, BMI, diabetic status, labor, and rupture of membranes to calculate the propensity score for each observation, which was the probability of receiving a particular antibiotics regimen. For the multiple treatment comparison, a multinomial logistic regression was used with the same independent variables to obtain more than one set of propensity score. The propensity score-adjusted logistic regression models were then conducted to estimate the effect of antibiotic regimens on the adverse outcomes, measured by adjusted odds ratios (OR) and the 95% confidence intervals.¹³ Specifically, we included the dummy variable indicating the treatment group and the propensity score as covariates. For the model estimating multiple treatment effects, the treatment groups, two propensity scores and their product term were included as covariates. The method was suggested when the study involves multiple treatment comparison, where matching and stratification on multiple propensity scores are difficult to conduct in clinical practice and may result in small treatment samples.¹³ Firth's penalized likelihood approach was applied in the regression models to address issues of rare events.^{14, 15} We then performed a subgroup analysis comparing women who received standard alternative or inappropriate alternative antibiotics with those who received cefazolin. Finally, we performed a sensitivity analysis by excluding women who delivered after routine azithromycin administration was implemented (since December 2016) as well as those with HIV and illicit drug use. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results:

There were 7,016 cesarean deliveries during the study period. Of these, 327 and 105 were excluded due to chorioamnionitis and lack of antibiotic information, respectively (Figure 1). Of 6,584 cases included in the analysis, 6,163 women (93.6%) received cefazolin. Of 421 women (6.4%) who received non-cephalosporin antibiotics, 274 (65.1%) and 147 (34.9%) received standard alternative and inappropriate alternatives, respectively. Among 274 women who received standard alternative antibiotics, 12 (4.4%) did not have beta-lactam allergy. The remaining 262 women had a history of beta-lactam allergy: a significant reaction in 138 (50.4%), no significant reaction in 87 (31.8%), and no specific allergic reaction was documented in 37 (13.5%). Among 147 women who received inappropriate alternative

antibiotics, 24 (16.3%) did not report a beta-lactam allergy. The remaining 123 women had a history of beta-lactam allergy: a significant reaction in 57 (38.8%), no significant reaction in 41 (27.9%), and no specific allergic reaction was documented in 25 (17.0%).

Maternal demographics and labor and delivery outcomes are presented in Table 1. Compared with women who received cefazolin, women who received non-cephalosporin antibiotics were more likely to be older, non-Hispanic white, deliver at earlier gestational age, use an illicit drug or have pregnancy-associated hypertension ($P<.05$).

The rates of maternal outcomes according to antibiotics type (cefazolin vs. non-cephalosporin) are presented in Table 2. Compared with cefazolin, use of non-cephalosporin antibiotics was associated with increased odds of the primary outcome (crude OR 2.43; 95%CI 1.73–3.40; adjusted OR 2.45; 95%CI 1.73–3.41), endometritis before discharge (crude OR 2.94; 95%CI 1.82–4.75; adjusted OR 3.37; 95%CI 2.04–5.35), endometritis after discharge (crude OR 4.40; 95%CI 1.99–9.75; adjusted OR 5.27; 95%CI 2.26–11.09), deep wound infection (crude OR 3.36; 95%CI 1.27–8.91; adjusted OR 3.61; 95%CI 1.26–8.72), cellulitis (crude OR 2.51; 95%CI 1.61–3.91; adjusted OR 2.33; 95%CI 1.46–3.57), and Emergency Department visit due to wound complication including infection, hematoma/seroma, or dehiscence (crude OR 2.14; 95%CI 1.29–3.54; adjusted OR 2.36; 95%CI 1.38–3.80). The sensitivity analysis after excluding women who delivered after routine azithromycin administration was implemented (since December 2016) as well as those with HIV and illicit drug use showed similar findings (Table S1).

We performed a subgroup analysis to further analyze if there is a difference in the primary outcome with standard alternative or inappropriate alternative antibiotics compared to cefazolin. The rates of maternal outcomes according to antibiotic type (cefazolin vs. standard alternative or inappropriate alternative antibiotics) are presented in Table 3. There was no difference in the primary outcome between women who received cefazolin and those who received standard alternative antibiotics. Use of standard alternative antibiotics was associated with increased odds of cellulitis (crude OR 2.07; 95%CI 1.16–3.70; adjusted OR 1.93; 95%CI 1.03–3.31) and Emergency Department visit due to wound complication (crude OR 2.00; 95%CI 1.07–3.76; adjusted OR 2.34; 95%CI 1.19–4.18) compared with cefazolin. In the sensitivity analysis, cellulitis was not statistically significant (crude OR 2.16; 95%CI 1.11–4.18; adjusted OR 2.01; 95%CI 0.98–3.70) (Table S2). Use of inappropriate alternative antibiotics compared with cefazolin was associated with increased odds of the primary outcome (crude OR 4.37; 95%CI 2.80–6.83; adjusted OR 4.13; 95%CI 2.59–6.36), endometritis before discharge (crude OR 6.85; 95%CI 3.94–11.90; adjusted OR 6.68; 95%CI 3.69–11.44), cellulitis (crude OR 3.36; 95%CI 1.78–6.34; adjusted OR 3.23; 95%CI 1.63–5.81), and Emergency Department visit due to wound complication (crude OR 2.40; 95%CI 1.10–5.22; adjusted OR 2.64; 95%CI 1.13–5.29). The sensitivity analysis showed similar findings (Table S2).

Discussion

In this large cohort of women undergoing cesarean delivery, we found that use of non-cephalosporin antibiotics was associated with increased odds of surgical site infections

compared with the use of cefazolin. We also found that use of standard alternative antibiotics (gentamicin and clindamycin) as recommended by ACOG¹¹ was associated with increased odds of cellulitis and Emergency Department visit due to wound complications compared with use of cefazolin. Use of inappropriate alternative antibiotics was associated with even higher odds of wound complications compared with use of cefazolin.

ACOG recommends prophylactic antibiotics for all women undergoing cesarean deliveries.¹¹ First-generation cephalosporin antibiotics are recommended as the antibiotic of choice unless significant drug allergy (anaphylaxis, angioedema, respiratory distress, or urticarial) is reported. ACOG recommends the combination of clindamycin with an aminoglycoside as a reasonable alternative for women with significant beta-lactam allergy¹¹ though efficacy data comparing the standard alternative antibiotics to cefazolin are limited. Although there was no difference in the primary outcome, we found that cellulitis was noted to be increased in association with standard alternative antibiotics compared to cefazolin. The increase in cellulitis may be explained by effectiveness of cefazolin in controlling skin flora such as *Streptococcus* species and *Staphylococcus* species compared to that of non-beta-lactam agents.¹⁶

In our study, 2.2% of women received a prophylactic antibiotic regimen that was not recommended by ACOG. The majority of those who received inappropriate alternative antibiotics received only a single agent of clindamycin or gentamicin alone. Our data found an even higher risk of wound complications with the use of inappropriate alternative antibiotics compared with cefazolin.

With this information in mind, clinicians need to assess the validity of a patient-reported history of beta-lactam allergy since only 10–20% of patients reporting a beta-lactam allergy demonstrate a true allergy when assessed by skin testing.¹⁷ To identify women with significant beta-lactam allergy, beta-lactam allergy skin testing (BLAST) as a point of care testing may be useful.¹⁸ This test has a negative predictive value of 97% in excluding a reaction to beta-lactam antibiotics and has been used in pregnant women.^{19, 20} A significant beta-lactam allergy was reported among 50% of women who received standard alternative and in 39% who inappropriate alternative antibiotics. Therefore, using cefazolin for women with a history of a non-significant beta-lactam allergy may lower the rate of post-cesarean wound complications.

Strengths of our study include a large sample of women and high-quality data from chart review. Our large sample size allowed us to examine differences in outcomes such as cellulitis, endometritis, and deep wound infection. We conducted a chart review of outpatient, inpatient, and anesthesia records and therefore, we believe our data are accurate. In using an objective definition of wound complication, we are confident that the rate of wound complications was not overestimated. Further, use of a propensity score analysis controlled potential imbalances.

Our study is limited in that our hospital is located in urban Washington, DC where the majority of women were non-Hispanic black; therefore, our study may not be generalizable in other settings. Explanations for administration of non-cephalosporin antibiotics were not

available, though our data showed 4% (12 women) and 16% (24 women) of women who received standard alternative and inappropriate antibiotics, respectively, did not have beta-lactam allergy. Of these, 25% (3/12) and 8% (2/24) had a fever of at least 38.0°C but not meeting criteria for a diagnosis of chorioamnionitis. Since none of these women developed surgical site infections, we do not believe the increased odds of having surgical site infections were merely due to undiagnosed chorioamnionitis. Some women may have gone to institutions outside of MedStar hospitals for care of wound complications, which would have been unrecognized by the chart review. However, this would be applied to all women, not just to women who received non-cephalosporin antibiotics. Finally, even though cellulitis was statistically significant, there was no difference in the primary outcome between women who received cefazolin and those who received standard alternative antibiotics. Given that some odds ratios were less than 3, associations were not strong and likely to be attributable to bias than causality.²¹ Larger studies are warranted to confirm our findings.

In conclusion, use of both standard alternative and inappropriate alternative antibiotics was associated with higher odds of surgical site infections compared with use of cefazolin for prophylaxis at the time of cesarean delivery. A thorough evaluation of patient-reported beta-lactam allergy and adherence to ACOG recommended antibiotic regimen may lower the rates of post-cesarean surgical site infections. Further studies that examine alternatives to ACOG recommended alternative antibiotics would be useful.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement:

Research reported in this publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR001409. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Reference:

1. Hamilton BE, Martin JA, Osterman MJK, et al. Births: Final data for 2014 National vital statistics reports; vol 64 no 12. Hyattsville, MD: National Center for Health Statistics 2015
2. Burrows LJ, Meyn LA, Weber AM. Maternal morbidity associated with vaginal versus cesarean delivery. *Obstet Gynecol.* 2004;103:907–12. [PubMed: 15121564]
3. Mackeen AD, Khalifeh A, Fleisher J, et al. Suture compared with staple skin closure after cesarean delivery: a randomized controlled trial. *Obstet Gynecol.* 2014;123(6):1169–75. [PubMed: 24807325]
4. Peleg D, Eberstark E, Warsof SL, et al. Early wound dressing removal after scheduled cesarean delivery: a randomized controlled trial. *Am J Obstet Gynecol.* 2016;215(3):388.e1–5. [PubMed: 27018465]
5. Blumenfeld YJ, El-Sayed YY, Lyell DJ, et al. Risk Factors for Prolonged Postpartum Length of Stay Following Cesarean Delivery. *Am J Perinatol.* 2015;32(9):825–32. [PubMed: 25594218]
6. Tita AT, Szychowski JM, Boggess K, et al. Adjunctive Azithromycin Prophylaxis for Cesarean Delivery. *N Engl J Med.* 2016;375(13):1231–41. [PubMed: 27682034]

7. Haas DM, Pazouki F, Smith RR, et al. Vaginal cleansing before cesarean delivery to reduce postoperative infectious morbidity: a randomized, controlled trial. *Am J Obstet Gynecol.* 2010;202(3):310.e1–6. [PubMed: 20207251]
8. Berg CJ, Chang J, Callaghan WM, et al. Pregnancy-related mortality in the United States, 1991–1997. *Obstet Gynecol.* 2003;101:289–96. [PubMed: 12576252]
9. Costantine MM, Rahman M, Ghulmiyah L, et al. Timing of perioperative antibiotics for cesarean delivery: a metaanalysis. *Am J Obstet Gynecol.* 2008;199(3):301.e1–6. [PubMed: 18771991]
10. Olsen MA, Butler AM, Willers DM, et al. Comparison of costs of surgical site infection and endometritis after cesarean delivery using claims and medical record data. *Infect Control Hosp Epidemiol.* 2010 8;31(8):872–5. [PubMed: 20583923]
11. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 120: Use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol.* 2011 6;117(6):1472–83. [PubMed: 21606770]
12. Higgins RD, Saade G, Polin RA, et al. Evaluation and management of women and newborns with a maternal diagnosis of chorioamnionitis. *Obstet Gynecol* 2016;127:426–36. [PubMed: 26855098]
13. Spreeuwenberg MD, Bartak A, Croon MA, et al. The multiple propensity score as control for bias in the comparison of more than two treatment arms: an introduction from a case study in mental health. *Med Care.* 2010 2;48(2):166–74. [PubMed: 20068488]
14. Firth D (1993), “Bias Reduction of Maximum Likelihood Estimates,” *Biometrika*, 80, 27–38.
15. Heinze G (2006), “A Comparative Investigation of Methods for Logistic Regression with Separated or Nearly Separated Data,” *Statistics in Medicine*, 25, 4216–4226. [PubMed: 16955543]
16. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect* 2013;14:73–156.
17. Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. *JAMA.* 2001 5 16;285(19):2498–505. [PubMed: 11368703]
18. Barlam TF, Cosgrove SE, Abbo LM, et al. Executive Summary: Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis.* 2016 5 15;62(10):1197–1202. [PubMed: 27118828]
19. Macy E, Mangat R, Burchette RJ. Penicillin skin testing in advance of need: multiyear follow-up in 568 test result-negative subjects exposed to oral penicillins. *J Allergy Clin Immunol.* 2003 5;111(5):1111–5. [PubMed: 12743578]
20. Macy E Penicillin skin testing in pregnant women with a history of penicillin allergy and group B streptococcus colonization. *Ann Allergy Asthma Immunol.* 2006 8;97(2):164–8. [PubMed: 16937745]
21. Grimes DA, Schulz KF. False alarms and pseudo-epidemics: the limitations of observational epidemiology. *Obstet Gynecol.* 2012 Oct;120(4):920–7.

Figure 1.
Cohort diagram

Table 1.

Demographics and labor and delivery outcomes

	Cefazolin (n=6,163)	Non-cephalosporin (n=421)	P-value
Maternal age, mean (SD) (n=6,161, n=421)	29.7 (6.3)	30.9 (6.0)	<.01
Nulliparas (n=6,145, n=418)	2,432 (39.6)	168 (40.2)	.80
Multiple gestation (n=6,161, n=421)	266 (4.3)	26 (6.2)	.07
Number of previous CD, median (10; 90th %tile) (n=6,163, n=421)	0 (0,2)	0 (0,2)	.63
Race/ethnicity			<.01
Non-Hispanic White	555 (9.0)	80 (19.0)	
Non-Hispanic Black	4,206 (68.3)	264 (62.7)	
Hispanic	538 (8.7)	29 (6.9)	
Asian/Pacific Islander	328 (5.3)	20 (4.8)	
Other	261 (4.2)	18 (4.3)	
Unknown	275 (4.5)	10 (2.4)	
BMI (kg/m ²), mean (SD) (n=6,091, n=420)	34.6 (7.9)	34.9 (8.5)	.37
GA at delivery, mean (SD) (n=6,153, n=421)	38.3 (2.8)	37.8 (3.1)	<.01
Smoking	269 (4.4)	26 (6.2)	.08
Alcohol use	73 (1.2)	8 (1.9)	.20
Illicit drug use	256 (4.2)	27 (6.4)	.03
Diabetes			.30
Pregestational diabetes	184 (3.0)	18 (4.3)	
Gestational diabetes	382 (6.2)	28 (6.7)	
Chronic hypertension	369 (6.0)	35 (8.3)	.05
Pregnancy-associated hypertension	1,030 (16.7)	89 (21.1)	.02
HIV	86 (1.4)	11 (2.6)	.04
Emergent cesarean delivery (n=6,161, n=421)	495 (8.0)	31 (7.4)	.75
Azithromycin	1032 (16.7)	67 (15.9)	.66
Skin preparation (n=6,162, n=421)			.66
No Prep due to stat cesarean	495 (8.0)	31 (7.4)	
Chlorhexidine	1,616 (26.2)	120 (28.5)	
Povidone iodine	4,044 (65.6)	270 (64.1)	
Both	7 (0.1)	0 (0)	
Vaginal preparation	667 (10.8)	47 (11.2)	.83
Vertical skin incision (n=6,158, n=419)	161 (2.6)	13 (3.1)	.56
Staple skin closure (n=6,159, n=421)	1,213 (19.7)	72 (17.1)	.19
Total operative time, mean (SD) (n=5,958, n=410)	49.4 (42.1)	50.6 (21.6)	.31
Labor (cervix 4cm + contraction)	2,660 (43.2)	169 (40.1)	.23
Second stage (n=6,161, n=421)	433 (7.0)	28 (6.7)	.77
Rupture of membranes (n=6,162, n=421)	2,603 (42.2)	165 (39.2)	.22
Duration of ROM (n=6,134, n=421)			.23
0.1 – 5.9 hours	1,021 (16.6)	62 (14.7)	
6.0 – 11.9 hours	719 (11.7)	37 (8.8)	

	Cefazolin (n=6,163)	Non-cephalosporin (n=421)	P-value
12 – 17.9 hours	382 (6.2)	31 (7.4)	
18 hours or longer	453 (7.4)	35 (8.3)	

Abbreviations: CD (cesarean delivery), BMI (body mass index), GA (gestational age), HIV (human immunodeficiency virus), Standard deviation (SD)

Number shown as n (%) unless otherwise specified.

Table 2. Maternal outcomes according to antibiotic type (cefazolin vs. non-cephalosporin) including women who received azithromycin

	Cefazolin (n=6,163)	Non-cephalosporin (n=421)	Crude OR (95%CI)	adjusted OR (95%CI)
Primary outcome (any of following) [†]	279 (4.5)	43 (10.2)	2.43 (1.73–3.40)	2.45 (1.73–3.41)
Endometritis before discharge [†]	108 (1.8)	21 (5.0)	2.94 (1.82–4.75)	3.37 (2.04–5.35)
Endometritis after discharge [†]	27 (0.4)	8 (1.9)	4.40 (1.99–9.75)	5.27 (2.26–11.09)
Deep wound infection [†]	22 (0.4)	5 (1.2)	3.36 (1.27–8.91)	3.61 (1.26–8.72)
Abdominopelvic abscess [†]	10 (0.2)	3 (0.7)	-	-
Maternal sepsis [†]	7 (0.1)	3 (0.7)	-	-
Cellulitis	145 (2.4)	24 (5.7)	2.51 (1.61–3.91)	2.33 (1.46–3.57)
Secondary outcome				
Henatoma or seroma [†]	84 (1.4)	11 (2.6)	1.94 (1.03–3.67)	1.92 (0.97–3.46)
Dehiscence (>1cm) [‡]	130 (2.1)	15 (3.6)	1.71 (1.00–2.95)	1.68 (0.94–2.80)
Emergency Department visit (any)	583 (9.5)	44 (10.5)	1.12 (0.81–1.54)	1.09 (0.78–1.49)
Emergency Department visit due to wound complications	126 (2.0)	18 (4.3)	2.14 (1.29–3.54)	2.36 (1.38–3.80)
Hospital readmission (any)	168 (2.7)	15 (3.6)	1.32 (0.77–2.26)	1.29 (0.73–2.14)

Abbreviations: OR (odds ratio), CI (confidence interval)

[†] n=6,162, n=421

[‡] n=6,161, n=421

Number shown as n (%) unless otherwise specified. Some analyses had too few observations to calculate ORs.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3.

Maternal outcomes according to antibiotic type (cefazolin vs. standard alternative or inappropriate alternative antibiotics) including women who received azithromycin

	Cefazolin (n=6,163)	Standard alternative (n=274)	Crude OR (95%CI)	adjusted OR (95%CI)	Inappropriate alternative (n=147)	Crude OR (95%CI)	adjusted OR (95%CI)
Primary outcome (any of following) [†]	276 (4.5)	18 (6.6)	1.50 (0.92–2.46)	1.63 (0.97–2.60)	25 (17.0)	4.37 (2.80–6.83)	4.13 (2.59–6.36)
Endometritis before discharge [†]	108 (1.8)	5 (1.8)	1.04 (0.42–2.58)	1.51 (0.55–3.31)	16 (10.9)	6.85 (3.94–11.90)	6.68 (3.69–11.44)
Endometritis after discharge [†]	27 (0.4)	4 (1.5)	-	-	4 (2.7)	-	-
Deep wound infection [†]	22 (0.4)	2 (0.7)	-	-	3 (2.0)	-	-
Abdominopelvic abscess [†]	10 (0.2)	2 (0.7)	-	-	1 (0.7)	-	-
Maternal sepsis [†]	7 (0.1)	1 (0.4)	-	-	2 (1.4)	-	-
Cellulitis	145 (2.4)	13 (4.7)	2.07 (1.16–3.70)	1.93 (1.03–3.31)	11 (7.5)	3.36 (1.78–6.34)	3.23 (1.63–5.81)
Secondary outcome							
Henatoma or seroma [†]	84 (1.4)	6 (2.2)	1.62 (0.70–3.74)	1.66 (0.67–3.48)	5 (3.4)	2.55 (1.02–6.38)	2.62 (0.96–5.80)
Dehiscence > 1cm [‡]	130 (2.1)	10 (3.6)	1.76 (0.91–3.38)	1.74 (0.86–3.17)	5 (3.4)	1.63 (0.66–4.05)	1.71 (0.63–3.73)
Emergency Department visit (any)	583 (9.5)	27 (9.9)	1.05 (0.70–1.57)	1.02 (0.66–1.50)	17 (11.6)	1.25 (0.75–2.09)	1.26 (0.73–2.04)
Emergency Department visit due to wound complication	126 (2.0)	11 (4.0)	2.00 (1.07–3.76)	2.34 (1.19–4.18)	7 (4.8)	2.40 (1.10–5.22)	2.64 (1.13–5.29)
Hospital readmission (any)	168 (2.7)	8 (2.9)	1.07 (0.52–2.20)	1.07 (0.49–2.04)	7 (4.8)	1.78 (0.82–3.87)	1.81 (0.79–3.62)

[†] n=6,162, 274, 147
[‡] n=6,161, 274, 147

Abbreviations: aOR (adjusted odds ratio), CI (confidence interval)

Number shown as n (%) unless otherwise specified. Some analyses had too few observations to calculate ORs.